

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
20 January 2005 (20.01.2005)

PCT

(10) International Publication Number  
**WO 2005/005431 A2**

(51) International Patent Classification<sup>7</sup>: **C07D 491/00**

(21) International Application Number:  
PCT/IT2004/000374

(22) International Filing Date: 6 July 2004 (06.07.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
RM 2003 A 000344 14 July 2003 (14.07.2003) IT

(71) Applicants (for all designated States except US):  
**SIGMA-TAU INDUSTRIE FARMACEUTICHE RI-  
UNITE S.p.A.** [IT/IT]; Viale Shakespeare, 47, I-00144  
Roma (IT). **ISTITUTO NAZIONALE PER LO STU-  
DIO E LA CURA DEI TUMORI** [IT/IT]; Via Venezian,  
1, I-20133 Milano (IT).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **GIANNINI,  
Giuseppe** [IT/IT]; c/o Simgma-Tau Industrie Farmaceu-  
tiche Riunite S.p. .A., Via Pontina, Km. 30,400, I-00040  
Pomezia (IT). **PENCO, Sergio** [IT/IT]; Via Milly Carla  
Mignone, 5, I-20153 Milano (IT). **TINTI, Maria, Ornella**  
[IT/IT]; c/o Simgma-Tau Industrie Farmaceutiche Riunite  
S.p. .A., Via Pontina, Km. 30,400, I-00040 Pomezia  
(IT). **PISANO, Claudio** [IT/IT]; c/o Simgma-Tau Indus-  
trie Farmaceutiche Riunite S.p. .A., Via Pontina, Km.  
30,400, I-00040 Pomezia (IT). **VESCI, Loredana** [IT/IT];  
c/o Simgma-Tau Industrie Farmaceutiche Riunite S.p.,  
.A., Via Pontina, Km. 30,400, I-00040 Pomezia (IT).  
**MERLINI, Lucio** [IT/IT]; c/o Simgma-Tau Industrie

Farmaceutiche Riunite S.p. .A., Via Pontina, Km. 30,400,  
I-00040 Pomezia (IT). **ZUNINO, Franco** [IT/IT]; c/o  
Istituto Nazionale per lo Studio e la Cura dei Tumori, Via  
Venezian, 1, I-20133 Milano (IT).

(74) Agents: **SPADARO, Marco** et al.; Cavattoni - Raimondi,  
Viale dei Parioli, 160, I-00197 Roma (IT).

(81) Designated States (unless otherwise indicated, for every  
kind of national protection available): AE, AG, AL, AM,  
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,  
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,  
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,  
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,  
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,  
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,  
ZW.

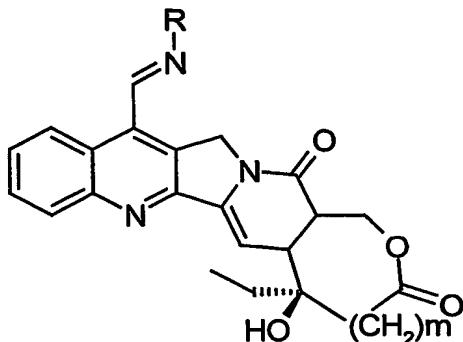
(84) Designated States (unless otherwise indicated, for every  
kind of regional protection available): ARIPO (BW, GH,  
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,  
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),  
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,  
FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,  
SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,  
GW, ML, MR, NE, SN, TD, TG).

**Published:**

— without international search report and to be republished  
upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

(54) Title: 7-POLYAMINOALKYL(OXY)IMINOMETHYLCAMPTOTHECINS BEARING PROTECTIVE GROUPS



(57) Abstract: Compounds are disclosed with the general formula (I) in which the groups are as defined in the description here below and characterized by the presence of polyamine substituents on the imine/oxime residue, such amine groups being in turn protected by suitable protective groups. Said compounds are endowed with potent topoisomerase I inhibiting activity and therefore are useful as medicaments for the treatment of tumours and viral and parasite infections.

WO 2005/005431 A2

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
20 January 2005 (20.01.2005)

PCT

(10) International Publication Number  
**WO 2005/005431 A3**

(51) International Patent Classification<sup>7</sup>: **C07D 491/22 //**  
(C07D 491/22, 491:22), 491:22), A61K 31/437,  
A61P 35/00

I-00040 Pomezia (IT). ZUNINO, Franco [IT/IT]; c/o  
Istituto Nazionale per lo Studio e la Cura dei Tumori, Via  
Venezian, 1, I-20133 Milano (IT).

(21) International Application Number:  
PCT/IT2004/000374

(74) Agents: SPADARO, Marco et al.; Cavattoni - Raimondi,  
Viale dei Parioli, 160, I-00197 Roma (IT).

(22) International Filing Date: 6 July 2004 (06.07.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
RM 2003 A 000344 14 July 2003 (14.07.2003) IT

(81) Designated States (unless otherwise indicated, for every  
kind of national protection available): AE, AG, AL, AM,  
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,  
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,  
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,  
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,  
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,  
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,  
ZW.

(71) Applicants (for all designated States except US):  
**SIGMA-TAU INDUSTRIE FARMACEUTICHE RI-**  
**UNITE S.p.A.** [IT/IT]; Viale Shakespeare, 47, I-00144  
Roma (IT). **ISTITUTO NAZIONALE PER LO STU-**  
**DIO E LA CURA DEI TUMORI** [IT/IT]; Via Venezian,  
1, I-20133 Milano (IT).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **GIANNINI,**  
**Giuseppe** [IT/IT]; c/o Simgma-Tau Industrie Farmaceu-  
tiche Riunite S.p. A., Via Pontina, Km. 30,400, I-00040  
Pomezia (IT). **PENCO, Sergio** [IT/IT]; Via Milly Carla  
Mignone, 5, I-20153 Milano (IT). **TINTI, Maria, Ornella**  
[IT/IT]; c/o Simgma-Tau Industrie Farmaceutiche Riunite  
S.p. A., Via Pontina, Km. 30,400, I-00040 Pomezia  
(IT). **PISANO, Claudio** [IT/IT]; c/o Simgma-Tau Indus-  
trie Farmaceutiche Riunite S.p. A., Via Pontina, Km.  
30,400, I-00040 Pomezia (IT). **VESCI, Loredana** [IT/IT];  
c/o Simgma-Tau Industrie Farmaceutiche Riunite S.p.  
.A., Via Pontina, Km. 30,400, I-00040 Pomezia (IT).  
**MERLINI, Lucio** [IT/IT]; c/o Simgma-Tau Industrie  
Farmaceutiche Riunite S.p. A., Via Pontina, Km. 30,400,

(84) Designated States (unless otherwise indicated, for every  
kind of regional protection available): ARIPO (BW, GH,  
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,  
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),  
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,  
FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,  
SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,  
GW, ML, MR, NE, SN, TD, TG).

**Published:**

- with international search report
- before the expiration of the time limit for amending the  
claims and to be republished in the event of receipt of  
amendments

(88) Date of publication of the international search report:  
24 February 2005

For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

(54) Title: 7-POLYAMINOALKYL(OXY)IMINOMETHYLCAMPTOTHECINS BEARING PROTECTIVE GROUPS

(57) Abstract: Compounds are disclosed with the general formula (I) in which the groups are as defined in the description here below and characterized by the presence of polyamine substituents on the imine/oxime residue, such amine groups being in turn protected by suitable protective groups. Said compounds are endowed with potent topoisomerase I inhibiting activity and therefore are useful as medicaments for the treatment of tumours and viral and parasite infections.

WO 2005/005431 A3